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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/519,436	12/22/2004	Hilde Azjin	TIP0015 US	7541

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EXAMINER	
HUMPHREY, LOUISE WANG ZHIYING	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 03/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/519,436	AZJIN ET AL.	
	Examiner	Art Unit	
	Louise Humphrey, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) *1,3,4 and 6-10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2 and 5* is/are rejected.

7)☒ Claim(s) *2 and 5* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The Office acknowledges the receipt of Applicant's election and Amendment, filed on 13 February 2006.

There was a cover letter filed on 23 February 2006 indicating the submission of an information disclosure statement (IDS) in the application. However, the form 1449 and copies of the references are missing. During a phone conversation with Attorney Alana Kriegsman on 6 March 2006, it was clarified that the IDS cover letter was typed with erroneous serial number and examiner information. The cover letter was intended for a different application. Therefore, Attorney Kriegsman confirms that this IDS cover letter should be disregarded and removed from the record for the instant application. Attorney further confirms that no IDS has been filed for the instant application.

Election/Restrictions

Applicant elects Group II, claims 2 and 5, with traverse.

Applicants merely stated that "the request is traversed as excessive" without further support. Because applicant did not distinctly and specifically point out any errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicants are no longer entitled to the rejoinder of the process claims with the product claims, *In re Ochiai* and *In re Brouwer*, because Applicant has elected the process claims.

The restriction among the different products that may be used in the claimed methods is maintained.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-10 are pending. Claims 1, 3, 4, and 6-10 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention/species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 13 February 2006.

Claims 2 and 5 are examined in the instant application.

Priority

No receipt is acknowledged of papers submitted under 35 U.S.C. §119(a)-(d). Therefore, the priority date is deemed to be the filing date of the priority application 60/393,025 (07/01/2002).

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Specification

The abstract of the disclosure is objected to because the title is included on the same page as the abstract. Correction is required. See MPEP § 608.01(b).

The title of the invention is objected to because it contains the word "new." A new title is required.

Claim Objections

Claim 2 is objected to because the space between the words "strain" and "comprising" is missing. Appropriate correction is required.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. §112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2 and 5 are rejected under 35 U.S.C. §112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: (1) determination of the effectiveness of a reverse transcriptase (RT) inhibitor; and (2) comparison of the drug effectiveness in samples containing the RT mutation, 194G, with samples not containing said mutation.

Clarification and/or correction are required.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2 and 5 are rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for evaluating the effectiveness of a reverse transcriptase inhibitor for HIV strains with a mutation at position 194 in the reverse transcriptase region, does not reasonably provide enablement for determining the susceptibility or effectiveness of other HIV drugs and other viral drugs in viral strains containing drug-resistant mutations at positions other than 194. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

"[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation.'" *Genentech Inc. v. Novo Nordisk* 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997); *In re Wright* 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); See also *Amgen Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed. Cir. 1991); *In re Fisher* 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Further, in *In re Wands* 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court stated:

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman* [230 USPQ 546, 547 (BdPatAppInt 1986)]. They include (1)

> the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).

The nature of the instant invention is a method for evaluating the effectiveness of a reverse transcriptase inhibitor as an antiviral therapy for a patient infected with at least one mutant HIV strain, or for evaluating a change in the viral drug susceptibility, comprising: (i) collecting a sample from an HIV-infected patient; (ii) determining whether the sample comprises a nucleic acid encoding HIV reverse transcriptase having at least one mutation 194G; (iii) correlating the presence of said at least one mutation of step (ii) to a change in effectiveness of said reverse transcriptase inhibitor or in viral drug susceptibility. The breadth of the instant claims is so broad that it encompasses all anti-viral drugs.

The guidance presented in the specification is limited to the detection of drug-resistant mutations at positions 194 in HIV reverse transcriptase. The specification does not provide the drug-resistance mutation profile for any viruses other than HIV. One skilled in the art cannot use the instant invention for other viral drugs because the

mutation at position 194 is specific for HIV reverse transcriptase but not other HIV enzymes or other viruses.

It is well known in the art that HIV is highly evolutionary and develops a wide spectrum of escape mutants (Shafer, 1999) towards not only reverse transcriptase inhibitors but also drugs acting at different sites in an HIV particle, such as protease inhibitors and fusion inhibitors. Due to this unpredictable nature, one skilled in the art would not be able to assess the susceptibility for all HIV drugs using only the single point mutation provided in the instant claims and specification.

Considering the lack of data or working examples in the specification, the broad scope of the claims, the complex state and nature of the art, and the teachings regarding unpredictability in this art, one skilled in the art would have to engage in an undue amount of experimentation to practice the invention as claimed. "Experimentation must not require ingenuity beyond that to be expected of one of ordinary skill in the art." See *Fields v. Conover*, 443 F.2d 1386, 170 USPQ 276 (CCPA 1970). In the instant case, detection of 194G mutation is not considered routine in successful screening for viral drug resistance in the art and, without sufficient guidance, the experimentation left to those skilled in the art is undue or unreasonable under the circumstances. It is noted that the unpredictability of a particular area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of claims. See *Ex parte Singh*, 17 USPQZd 1714 (BPAI 1991).

The instant invention, based on the evidence as a whole, in light of the factors articulated by the court in *In re Wands*, lacks an enabling disclosure.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 2 and 5 are rejected under 35 U.S.C. §103(a) as being unpatentable over Stein *et al.* (1994) in view of Servais (2001).

The instant claims read on a method for evaluating the effectiveness or susceptibility of a reverse transcriptase inhibitor for a patient infected with at least one mutation 194G.

Stein *et al.* discloses sequence analysis of HIV RT from HIV patients comprising collecting a sample from an HIV-infected patient; determining whether the sample comprises a nucleic acid encoding HIV reverse transcriptase having at least one mutation at position 194; and correlating the presence of the mutations to a change in effectiveness or susceptibility of AZT, a reverse transcriptase inhibitor.

Stein *et al.* does not disclose the specific amino acid change to G at position 194.

Servais discloses that the 194G mutation is found in the patient isolates in an assay for HIV-1 drug resistance mutations.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the drug-resistance mutation profiles taught by Stein *et al.* and Servais such that the modified method has a more

comprehensive mutation profile. One having ordinary skill in the art would have been motivated to do this so that the new mutation profile contributes to a more complete and accurate drug evaluation. Thus, claims 2 and 5 are obvious over Stein *et al.* in view of Servais.

Remarks

No claim is allowable.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise Humphrey, Ph.D., whose telephone number is 571-272-5543. The examiner can normally be reached on Mon-Fri, 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902.

Louise Humphrey, Ph.D.
Patent Examiner
1 March 2006

JEFFREY STUCKER
PRIMARY EXAMINER